II. REMARKS/ARGUMENTS

A. Status of the Claims

Claim 1, 3-8, 10-16 are currently pending in the present application. Claims 2 and 9 have been cancelled without prejudice. Claims 1, 4, 7, 10-12, and 14 have been amended without prejudice. New claims 41-45 have been added. Support for new claim 41 can be found e.g., at page 3, lines 5-7, and throughout the specification; and support for new claims 42-45 can be found e.g., in the original claims and throughout the specification. It is respectfully submitted that no new matter has been added by virtue of the present amendment.

B. Rejections under 35 U.S.C. § 112

Claims 1-9 and 13-16 were rejected under 35 U.S.C. § 112, first paragraph, by the Examiner "for scope of enablement because the specification, while being enabling for the particular agents such as HMG-COA reductase inhibitor selected from the group consisting of mevastatin, pravastatin, simvastatin, atolwastatin, lovastatin, rivastatin, fluvastatin disclosed in the specification (see page 51-59) employed in methods for treatments for Alzheimer's disease, does not reasonably provide enablement for the employment [of] any therapeutic agent which lowers Aβ levels, any HMG-COA reductase inhibitors, any NSAID, or any secretase inhibitors, or combination thereof, to be administered for the claimed methods of the particular treatments herein, i.e., Alzheimer's disease in a patient." The Examiner further states that "[t]hese recitations, 'a therapeutic agent which lowers Aβ levels', 'an HMG-COA reductase inhibitor', a 'secretase inhibitor', in these claims, are seen to be merely functional language." Additionally, the Examiner states that "[t]he instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***."

This rejection is traversed. Claim 1 has been amended to include the term "HMG CoA reductase inhibitor" in place of the term "therapeutic agent".

Initially, it is noted that the term HMG CoA reductase inhibitor is not merely functional language, but is representative of a known class of drugs with an art recognized mechanism of action which are antilipemic agents.

It is well recognized that "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988); MPEP 2164.01 (8th Edition, Rev. No. 1).

In addition, "[f]or a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation" MPEP 2164.02 (8th Edition, Rev. No. 1).

Therefore, the Applicants are not required to exemplify every HMG CoA reductase inhibitor which would be encompassed by the claim. If the application provides sufficient guidance for one of ordinary skill in the art to manipulate formulations proposed by the disclosure of the present application then the claim is enabled.

In the present application, Applicants are claiming "[a] method of managing a patient with Alzheimer's disease or at risk of developing Alzheimer's disease comprising: administering to said patient a HMG CoA reductase which lowers Aβ levels, and detecting a level of Aβ in a body fluid . . . ." Applicants have provided certain representative examples of the formulations, the effects of certain HMG CoA reductase inhibitors on the effects of Aβ in the present application, and have stated in the specification a number of HMG CoA reductase inhibitors useful in accordance with the present invention. The Examiner's attention is directed to the specific formulations represented in Tables 1 through 8 of the present application, the definition of the term

HMG CoA reductase inhibitor at page 11, line 32 to page 12, line 6, the listing of certain HMG CoA reductase inhibitors at page 12, lines 8-18, and the Human Trials in Example 4, the Aβ assays in Example 5, and percentage change from baseline results in Example 6.

In addition, the Examiner's attention is further directed to new dependent claims 41-44 which are directed to dosage ranges of the HMG-CoA reductase inhibitor, which are supported by the present specification, and which would further apprise one of ordinary skill in the art of the HMG-CoA inhibitor for use in accordance with the present invention.

In view of the present specification, and the amendments to the claims to specifically to a HMG CoA reductase inhibitor, it is respectfully submitted that the claimed genus of an HMG CoA reductase inhibitor could be used in the manner claimed without undue experimentation.

The Examiner is reminded that "Nothing more than objective enablement is required, and therefore, it is irrelevant whether [a] teaching is provided broad terminology or illustrative examples." *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Applicants have provided in the specification a comprehensive listing of representative HMG-CoA reductase inhibitors, formulations for including the HMG-CoA reductase inhibitors, Examples including clinical studies that support the present claims, and dosage ranges for the HMG-CoA reductase inhibitors. As these recitations are known in the art, or could be understood and comprehended by one skilled in the art, it is respectfully submitted that the present application provides objective enablement of the present method claims which recite "HMG-CoA Reductase Inhibitors."

It is respectfully submitted that all of the issues raised by the Examiner under 35 USC §112, first paragraph have now been addressed and have been overcome. It is respectfully requested that this rejection now be removed.

C. Rejections under 35 U.S.C. § 103

Claims 1-16 were rejected under 35 U.S.C. 103(a) as being "unpatentable over Scolnick (WO 95/06470, PTO-892) in view of Applicant's admission regarding the prior art in the specification (see page 7-8).

This rejection is traversed. Scolnick describes methods of administering HMG-CoA reductase inhibitors in order to lower ***ApoE isoform 4*** in the central nervous system to purportedly treat, arrest the development of and prevent the onset of Alzheimer's disease. Scolnick fails to recognize and provides no information regarding the level of Aβ being useful as an indicator as to the progression of Alzheimer's disease. Therefore, Scolnick fails in the very least to teach, hint, or suggest "detecting a level of Aβ in a body fluid of said patient to determine the efficacy of said HMG CoA reductase inhibitor" as recited in the present claims. It is respectfully submitted that in view of Scolnick, one would not be motivated to detect a level of Aβ to determine the efficacy of a therapeutic agent in treating Alzheimer's disease as the reference fails to appreciate or acknowledge that the Aβ level is useful as an indicator of such treatment as recited in the present claims.

The Examiner relies on Scolnick in combination with Applicants alleged admission of the prior art that "[a]ny procedures known in the art for the measurement of β-amyloid levels can be used in the practice of the instant invention", and that "[s]uch procedures include but are not limited to competitive and non-competitive assay systems using techniques such as radioimmunosassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, precipitin reactions, gel diffusion precipitin reactions . . . ." However, the knowledge that a procedure for measurement of Aβ exists does not in and of itself provide motivation to substitute it for the ApoE isoform 4 measurement in

Scolnick. Nor does Scolnick provide any hint or suggestion that a different test would be useful. Without providing the necessary motivation, the Examiner's rejection must fail and must be removed.

The Examiners' attention is directed to the language of *In re Lee*, 61 USPQ2d 1430 (Fed. Cir. 2002), which states the following concerning whether there is a teaching, motivation, or suggestion to select and combine references relied on as evidence of obviousness:

> "The factual inquiry whether to combine references must be thorough and searching." *Id.* It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with. *See, e.g., Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1124-25, 56 USPQ2d 1456, 1459 (Fed. Cir. 2000) ("a showing of a suggestion, teaching, or motivation to combine the prior art refereces is an 'essential component of an obviousness holding' ") (quoting *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1352, 48 USPQ2d 1614, 1617 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."); *In re Dance*, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) (there must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant); *In re Fine*, 837 F.2d 1071, 1075, 5USPQ2d 1596, 1600 (Fed. Cir. 1988) (" 'teachings of references can be combined *only* if there is some suggestion or incentive to do so.' ") (emphasis in original) (quoting *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984).

While any procedure known in the art for the measurement of Aβ levels can be used in the practice of the present invention as acknowledged in the present specification, the Examiner has failed to provide any motivation to one skilled in the art to detect Aβ levels in order to determine the efficacy of the HMG-CoA reductase inhibitor as recited in the present claims. It is respectfully submitted as Scolnick describes the detection ApoE isoform 4 levels there is no motivation to modify Scolnick in view of Applicants alleged admission to arrive at the presently claimed invention which recites ". . .

detecting a level of Aβ in a body fluid of said patient to determine the efficacy of said HMG CoA reductase inhibitor in reducing said Aβ level in said patient.

Therefore, the Examiner is respectfully requested to remove this rejection over Scolnick in view of Applicant's admission regarding the prior art in the specification.

D. Conclusion

It is now believed that the above-rejections have been obviated and withdrawal is respectfully requested. It is believed that all claims are now in condition for allowance.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,
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